A2 cont'd

maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 22.

Please amend page 4, lines 18-22 of the specification as follows:

A3

Figure 2 provides a chimeric oligonucleotide comprising three intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting one nucleotide at each of two amino acid residues of the target sequence. The linear (SEQ ID NO: 2) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 23.

Please amend page 4, lines 23-27 of the specification as follows:

A4

Figure 3 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting two nucleotides at each of two amino acid residues of the target sequence. The linear (SED ID NO: 3) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 23.

Please amend page 4, lines 28-32 of the specification as follows:

A5

Figure 4 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting one nucleotide at each of two amino acid residues of the target sequence. The linear (SEQ ID NO: 4) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 23.

Please amend pages 4 and 5, lines 33-34 and 1-4, respectively, of the specification as follows:

A6

Figure 5 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting two nucleotides at each of two amino acid residues of the target sequence. The first amino acid residue target is within a DNA region while the second amino acid residue target is within an RNA region. The linear (SEQ ID NO: 5) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 22.

Please amend page 5, lines 5-10 of the specification as follows:

A7

Figure 6 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting one nucleotide at each of two amino acid residues of the target sequence. The first amino acid residue target is within a DNA region while the second amino acid residue target is within an RNA region. The linear (SEQ ID NO: 6) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 24.

Please amend page 5, lines 11-16 of the specification as follows:

A8

Figure 7 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting two nucleotides at each of two amino acid residues of the target sequence. The first amino acid residue target is within an RNA region while the second amino acid residue target is within a DNA region. The linear (SEQ ID NO: 7) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 22.

Please amend page 5, lines 17-22 of the specification as follows:

A9

Figure 8 provides a chimeric oligonucleotide comprising two intervening blocks of RNA residues for modification of the maize EPSPS gene to a herbicide resistant form of the gene by converting one nucleotide at each of two amino acid residues of the target sequence. The first amino acid residue target is within an RNA region while the second amino acid residue target is within a DNA region. The linear (SEQ ID NO: 8) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 24.

Please amend page 5, lines 23-27 of the specification as follows:

A10

Figure 9 provides a chimeric oligonucleotide for a single amino acid modification of the maize EPSPS gene to a herbicide resistant form of the gene. The amino acid target here corresponds to the first of the two amino acid residues targeted by the chimeric oligonucleotides in Figures 1-8. The linear (SEQ ID NO: 9) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 25.

Please amend page 5, lines 28-32 of the specification as follows:

A11

Figure 10 provides a chimeric oligonucleotide for a single amino acid modification of the maize EPSPS gene to a herbicide resistant form of the gene. The amino acid target here corresponds to the second of the two amino acid residues targeted by the chimeric oligonucleotides in Figures 1-8. The linear (SEQ ID NO: 10) and active forms of the oligonucleotide are provided. A fragment of the maize EPSPS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 26.

Please amend pages 5 and 6, lines 33-34 and 1-2, respectively, of the specification as follows:

A12

Figure 11 provides a chimeric oligonucleotide for a single amino acid modification at amino acid position 621 of the maize AHAS gene to a herbicide resistant form of the gene. The linear (SEQ ID NO: 11) and active forms of the oligonucleotide are provided. A fragment of the maize AHAS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 27.

Please amend page 6, lines 3-6 of the specification as follows:

A13

Figure 12 provides a chimeric oligonucleotide for a single amino acid modification at amino acid position 165 of the maize AHAS gene to a herbicide resistant form of the gene. The linear (SEQ ID NO: 12) and active forms of the oligonucleotide are provided. A fragment of the maize AHAS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 28.

Please amend page 6, lines 7-10 of the specification as follows:

A14

Figure 13 provides a chimeric oligonucleotide for a single nucleotide modification which converts a stop codon to a codon encoding tyrosine in a transgene target previously introduced into maize (see text). The linear (SEQ ID NO: 13) and active forms of the oligonucleotide are provided. A fragment of the maize AHAS amino acid sequence is translated beneath the active oligonucleotide and is set forth in SEQ ID NO: 29).

Please amend page 17, lines 12-28 of the specification as follows:

A15

For the transgene target a translational fusion between phosphinothricin-N-acetyltransferase, *pat* (Wohlleben *et al.* (1988) *Gene 70*:25-37) and the green fluorescence protein, GFP (Prasher *et al.* (1992) *Gene 111*:229-233) was created. *pat* is a functional analog of the *bar* gene that similarly detoxifies Bialaphos. The coding sequences of GFP and *pat* have been modified to utilize maize preferred codons to enhance expression, these modified genes are referred to as GFPm and mo-PAT respectively. See, for example, U.S. application 09/003,287. A fusion was initially created by cloning the 3' Bg1II site in mo-PAT to a 5' flanking BamHI site

A15 cont'd

on GFPm. Site directed mutagenesis (MORPH kit, 5'-3' Boulder, CO) was then used to remove the start codon (ATG) from GFPm to ensure low background expression of GFPm in target lines. Using the oligonucleotide PHN14593, 5'CGGTGACGCAGATCTATCCAACATTGTCCAAGGGC3' (SEQ ID NO: 14), the Bg1II site was recreated in mo-PAT and the start codon of GFPm was removed simultaneously. Four amino acids, YPTS, form the junction in the mo-PAT/GFPm sequence. The vector pPHP10699, is a positive control mo-PAT/GFPm fusion cloned under the control of the maize Ubiquitin-1 promoter and pinII terminator in a pUC-derived plasmid backbone.

Please amend pages 17 and 18, lines 29-34 and 1-6, respectively, of the specification as follows:

A16

To create the target sequence for correction, the native *pat* stop codon (TGA) was inserted in the junction of mo-PAT/GFPm. Site-directed mutagenesis of pPHP10699 with oligonucleotide PHN16214, 5'GGTGACGCAGATCTAGGTACCATCGTCCAAGGGCGAG3' (SEQ ID NO: 15), was used to change the junction sequence from YPTS to *VPS and to introduce a *KpnI* site adjacent to the stop codon. This creates a sequence that only expresses mo-PAT, but with correction to remove the stop codon, GFPm expression results. When making corrections to this target, changing the TAG stop codon to TAC also knocks out the *KpnI* site and creates a novel *Sna*BI site. The vector pPHP11207, contains the mo-PAT/TAG/GFPm target sequence, cloned with the maize Ubiquitin-1 promoter and pinII terminator, and inserted into a superbinary vector pSB1 for *Agrobacterium* mediated transformation of maize (Ishida *et al.* (1996) *Nature Biotech. 14*:745-750).

Please amend page 20, lines 16-30 of the specification as follows:

A17

PCR amplification and sequence analysis - Target sequences were amplified from the extracted genomic DNA of putative events, by *Pwo* or *Taq* polymerase (Boehringer Mannheim, Indianapolis, IN) with 30 cycles of 35 seconds at 95°C, 35 seconds at 60°C, and 35 seconds at 72°C using a MJ thermocycler (MJ Research, Watertown, MA). For the AHAS621 target,

primers common to both AHAS108 and AHAS109 were designed with the following sequences: 5'GCAGTGGGACAGGTTCTAT (PHN21971) (SEQ ID NO: 16) and 5'AGTCCTGCCATCACCATCCA (PHN21972) (SEQ ID NO: 17). For the AHAS165 target, the following primers were used: 5'ACCCGCTCCCCCGTCAT (PHN21973) (SEQ ID NO: 18) and 5'ATCTGCTGCTGGATGTCCTTGG (PHN21974) (SEQ ID NO: 19). For the moPAT/GFPm target, primers used were: 5'CGCAACGCCTACGACTGGA (PHN21976) (SEQ ID NO: 20) and 5'TGATGCCGTTCTTCTGCTTGTC (PHN21978) (SEQ ID NO: 21). PCR fragments were purified and either cloned (see below) or directly sequenced in both directions on an ABI 377 automated sequencer.

In the Claims

Please amend the claims as follows:

1. (Amended) A method to inactivate a gene introduced into a genome of a plant cell, said method comprising:

transforming said plant cell with a nucleic acid molecule comprising a promoter operably linked to a nucleotide sequence comprising said gene;

introducing into said plant cell at least one chimeric oligonucleotide, said chimeric oligonulceotide having at least a first block of RNA residues and a second block of RNA residues, wherein said first and said second blocks of RNA residues are homologous to said nucleic acid molecule and flank a block of DNA residues, said chimeric oligonucleotide being capable of recognizing and implementing a nucleotide conversion in said nucleic acid molecule.

3. (Amended) The method of claim 1, wherein said nucleotide conversion is in the coding region of said gene.

Please add the following new claims:

9. The method of claim 5, wherein said herbicide resistance gene is a 5-enol pyruvylshikimate-3-phosphate synthase gene.

10. The method of claim 5, wherein said herbicide resistance gene is an acetohydroxy acid synthetase gene.

11. The method of claim 9, wherein said chimeric oligonucleotide is selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10.

12. The method of claim 10, wherein said chimeric oligonucleotide is selected from the group consisting of SEQ ID NO: 11, 12, and 13.

13. The method of claim 1, wherein said plant cell is from a monocot.

14. The method of claim 13, wherein said monocot is maize.

15. The method of claim 1, wherein said plant cell is from a dicot.

16. A method to inactivate a gene introduced into a genome of a plant, said method comprising:

transforming said plant with a nucleic acid molecule comprising a promoter operably linked to a nucleotide sequence comprising said gene;

introducing into said plant at least one chimeric oligonucleotide, said chimeric oligonulceotide having at least a first block of RNA residues and a second block of RNA residues, wherein said first and said second blocks of RNA residues are homologous to said

nucleic acid molecule and flank a block of DNA residues, said chimeric oligonucleotide being capable of recognizing and implementing a nucleotide conversion in said nucleic acid molecule.

17. The method of claim 16, wherein said nucleotide conversion is in the promoter.

18. The method of claim 16, wherein said nucleotide conversion is in the coding region of said gene.

19. The method of claim 16, wherein the chimeric oligonucleotide introduces a frameshift in the normal reading frame of the gene.

20. The method of claim 16, wherein the chimeric oligonucleotide introduces a premature stop codon in the normal reading frame of the gene.

21. The method of claim 16, wherein said gene is a marker gene.

22. The method of claim 16, wherein said gene is a herbicide resistance gene.

23. The method of claim 22, wherein said herbicide resistance gene is a 5-enol pyruvylshikimate-3-phosphate synthase gene.

24. The method of claim 22, wherein said herbicide resistance gene is an acetohydroxy acid synthetase gene.

25. The method of claim 23, wherein said chimeric oligonucleotide is selected from the group consisting of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10.

26. The method of claim 25, wherein said chimeric oligonucleotide is selected from the group consisting of SEQ ID NO: 11, 12, and 13.

27. The method of claim 16, wherein said plant is a monocot.

28. The method of claim 27, wherein said monocot is maize.

29. The method of claim 16, wherein said plant is a dicot.

REMARKS

Status of the Claims

Claims 1-8 were rejected. Claims 9-29 have been added. Claims 1-29 are pending in the present application.

Claim 1 has been amended to correct antecedent basis and to more clearly define the invention. Support for these amendments can be found throughout the specification and in the originally filed claims.

Claim 3 has been amended to have proper antecedent basis. Support for this amendment can be found throughout the specification and in the originally filed claims.

Claims 9-15 have been added. Claims 9 and 10 further recite that the herbicide resistance gene is an EPSPS or an AHAS gene, respectively. Support for these claims can be found, for example, on page 9, lines 31-34, Example 1, and Example 2. Claim 11 further recites that the chimeric oligonucleotide is selected from SEQ ID NOS: 1-10. Support for this claim can be found throughout the specification, for example, on pages 4-5, Example 1, and in SEQ ID NOS: 1-10. Claim 12 recites that the chimeric oligonucleotide is selected from SEQ ID NOS: 11 and 12. Support for this claim can be found, for example, on pages 5-6, Example 2, and in SEQ ID NOS: 11 and 12. Claims 13 and 15 recite that the plant cell is a monocot and a dicot, respectively. Support for these claims can be found, for example, on page 10, lines 19-21.